A*02 in Southern Thai Muslims and Central Thais

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Abstract

The HLA-A*02 subtyping in Thais was conducted and included in the 12th International Histocompatibility Workshop (12WS). A total of 81 randomized individuals previously serologically or DNA typed as A2 were studied for A2 subtypings. The subjects consisted of 32 Southern Thai-Muslims (STM) and 49 Central Thais (CT). The 12WS HLA-A*02 subtyping DNA typing kit was employed. The most common A*02 subtypes in STM were A*0203,*0201 and *0207 while they were A*0203,*0207 and *0201 in CT. A*0202, *0204, *0208, *0209, *0212, *0213, *0214, *0215, *0216 and *0217 were not found in both STM and CT. The 12WS data indicated that A*0201 was also the most frequent allele of A*2 among North-East Asians. A2 subtype study in 32 STM revealed that 2 in 8 of A*0201 showed the absence of bands at 813 bp and 705 bp with primer mix number 03A and 517A and weak reaction band with primer mix number 33A. In addition, 3 subjects with A*0201 variations have one nucleotide difference in exon 2 by sequence base typing (by MGJ. Tilanus) which will be reported separately. Conclusion : More variations of A*02 were observed among STM compared to CT. The variations of reactions with the set of primer mix should be carefully observed and subjected to further analysis.

The serological splits of A2 have been officially recognized since the 11th International Histocompatibility Workshop and Conference(1). Certain A2 subtypes such as A*0203 were found predominately in the Oriental and South-East Asian population(2).

Objective : This study was aimed to elucidate the A2 subtypes in Thais.

MATERIAL AND METHOD

Eighty-one randomized A2 individuals were included in this study which consisted of 32 Southern Thai Muslims (STM) from Nakhon Si Thammarat province whose ancestors were mostly from Malaysia(3) and 49 Central Thais (CT) who are of Chinese descent.

The 12th Workshop (WS) HLA-A*02.SSP ARMS-PCR subtyping kit was employed which

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included the class I ARMS - SSP primer mixes : 12WS-03A, 12WS-25A to 12WS-32A (9 primer mixes) as well as A*02 subtype first round primer mixes : 12WS-33A to 12WS-36A (4 primer mixes) and A*02 nested subtyping primer mixes : 12WS-501A to 12WS-519A (19 primer mixes). The method used was Amplification Refractory Mutation System (ARMS)[4].

The significance of the linkage disequilibrium between allele was tested using Chi-square analysis.

RESULTS

A*02 subtypes found in this study for CT were A*0201, A*0203, A*0206, A*0207, A*0210, A*0211, while they were A*0201, A*0203, A*0205, A*0206, A*0207, and A*0211 for STM.

The most common A*02 subtypes in CT were A*0203, A*0207 and A*0201 while they were A*0203, A*0201 and A*0207 in STM. The rare A*02 alleles in CT were A*0210, and A*0211 and in STM were A*0206, and A*0211, respectively.

A*0201 reaction patterns with the 12th WS set of primer mix are shown in Table 1. There was a variation observed in STM which was characterized by the absence of bands at 813 bp and 705 bp with primer mix number 03A and 517 A and weak reaction band with primer mix number 33A. This variation was found in 2 out of 8 of A*0201 STM. Three subjects with A*0201 variations had one nucleotide difference in exon 2 by sequence base typing by MGJ. Tilanus[5]. In this study, 3 individuals were homozygous and another 3 were heterozygous for A*0203/*0207 (N=2) and A*0201/*0205 (N=1), in STM, while 3 individuals were homozygous and 7 were heterozygous for A*0201/*0206 (N=2), A*0203/*0207 (N=3), A*0201/*0203 (N=1) and A*0201/*0207 (N=1) in CT. The significant association (haplotype frequency > 2 per cent, linkage disequilibrium > 2, and p value < 0.05) was found only in CT for A*0207-B46, A*0203-B60 and A*0201-B60, while significant association between A*02 with other antigens of classes I and II was not observed in STM (Table 2).

DISCUSSION

The ARMS PCR is a method for the rapid detection of single base pair changes or small deletions in DNA[5].

The variations of HLA - A*02 alleles detected by ARMS -PCR had been previously demonstrated in 3 different population groups including the Singapore Chinese population (Table 3)[6]. The profile of HLA - A*02 allelic frequency amongst CT was comparable with what had been observed in Singapore Chinese, except for A*0203 and A*0207. There were equally most common A*02 alleles in CT, while it was only A*0207 in Singapore Chinese[6]. A*0202 and A*0211 are rare A*02 subtypes in all Asian population (Table 4).

Table 1. Characteristics of A*0201 and its variations with 12th WS Primer Mix.

	Class I- ARMS-SSP									A2 Subgroup ARMS-SSP																									
														5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5
Specificity	0	2	2	2	2	2	3	3	3	3	3	3	3	0	0	0	0	0	0	0	0	0	1	1	1	1	1	1	1	1	1	1	1	1
	3	5	6	7	8	9	0	1	2	3	4	5	6	1	2	3	4	5	6	7	8	9	0	1	2	3	4	5	6	7	8	9	0	1
	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A
A*0201	+	+	-	-	-	-	-	-	+	+	-	-	+	+	-	-	-	-	-	-	-	-	-	-	-	-	-	-	+	-	+	-	-	-
A*0201 variant	-	+	-	-	-	-	-	-	+	W	-	-	+	+	-	-	-	-	-	-	-	-	-	-	-	-	-	-	+	-	-	-	-	-

Table 2. Occurence of homozygous, heterozygous and significant association of A*02 with other antigens of classes I and II.

	STM	CT
- Homozygous	3/32	3/49
	A*0203 (x 2)	A*0207 (x 1)
	A*0201 (x 1)	A*0203 (x 1)
		A*0206 (x 1)
- Heterozygous	3/32	7/49
	A*0203/0207 (x 2)	A*0201/0206 (x 2)
	A*0201/0205 (x 1)	A*0203/0207 (x 3)
		A*0201/0203 (x 1)
		A*0201/0207 (x 1)
- Sig. Assoc.	Non-Sig.	A*0207-B46 (7/13)
		A*0203-B60 (6/21)
		A*0201-B60 (4/9)

Sig. Assoc. = Significant Association : Haplotype frequency > 2%,
linkage disequilibrium > 2 and $p < 0.05$

Table 3. A*02 in CT and STM as compared to NET, C and SC (12IHW).

Alleles	C** N=63	SC** N=55	CT N=49	STM N=32	NET* N=48
*0201	73	15	9	8	-
*0203	-	15	21	15	24
*0205	1	-	-	3	1
*0206	-	5	8	1	1
*0207	-	30	13	7	25
*0210	-	1	1	-	-
*0211	1	-	1	1	-
*0213	1	-	-	-	-
Total	76	66	53	35	51

* Urwijitaroon et al. 12IHW ** Krausa et al,
C=Caucasian; SC=Singapore Chinese; CT=Central Thais; STM=Southern Thai Muslims; NET=North-Eastern Thais.

Table 4. A*02 alleles found in STM as compared to NET and North-East Asian.

					Chinese*		
Alleles	STM	NET**	Mongolian*	Buryat*	Man	Korean	Japanese*
A*0201	4.2	0.0	15.0	21.0	17.0	20.0	10.6
A*0202	0.0	0.0	0.0	0.5	0.0	0.0	0.0
A*0203	8.0	12.9	1.0	0.0	4.0	1.0	0.0
A*0205	1.5	0.5	4.0	5.5	0.5	0.0	0.0
A*0206	0.5	0.5	7.5	3.5	8.0	6.0	8.4
A*0207	3.4	12.7	1.0	1.0	5.5	3.0	4.0
A*0211	0.5	0.0	0.0	0.0	0.0	0.0	0.0
Total	18.6	26.6	28.5	31.5	35.0	30.0	23.0

* Juji et al. 12WS data ** Urwijitaroon et al. 12WS data

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A*02 ในคนไทยมุสลิมภาคใต้ และ คนไทยภาคกลาง

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ได้ศึกษา HLA-A*02 subtypes ของคนไทยใน 12th Histocompatibility Workshop (12WS) ทั้งหมดจำนวน 81 คน โดยสุ่มตัวอย่างจากผู้ซึ่งเคยตรวจมาก่อนว่าเป็น A2 ด้วยวิธี serology หรือวิธี DNA typing ในกลุ่มที่ศึกษาประกอบด้วยคนไทยมุสลิม ภาคใต้จากจังหวัดนครศรีธรรมราช (STM) จำนวน 32 คน และคนไทยมีเชื้อสายจีน ในภาคกลาง (CT) จำนวน 49 คน ใช้ 12th International Workshop (12WS) HLA-A*02 subtyping DNA typing kit ผลการศึกษา A*02 subtype ที่พบมากที่สุดและรองลงไปตามลำดับใน STM ได้แก่ A*0203, *0201 และ *0207 ส่วนใน CT ได้แก่ A*0203, *0207 และ *0201. A*02 ที่ไม่พบทั้งใน STM และ CT ได้แก่ A*0202, 0204, *0208, *0209, *0212, *0213, *0214, *0215, *0216 และ *0217 เมื่อเปรียบเทียบกับข้อมูลจาก 12WS พบว่า A*0201 เป็น subtype ของ A*02 ที่พบได้บ่อยในกลุ่ม North-East Asian ด้วย พบว่า 2 ใน 8 ราย ของ A*0201 มี variations ใน STM คือไม่มี bands ที่ 813 bp และ 705 bp กับ Primer Mix number 03A และ 517A และมี band จาง ๆ กับ primer mix number 33A เมื่อศึกษา STM 3 ราย ที่มี A*0201 variants เพิ่มเติมโดย Prof. MGJ. Tilanus พบว่ามีความแตกต่างของ nucleotide ใน exon 2 อยู่ หนึ่งตำแหน่ง เมื่อทำ sequence base typing ซึ่งจะรายงานแยกภายหลัง สรุป A*02 ใน STM มีความหลากหลายมากกว่าใน CT ความแตกต่างของผลในการศึกษา HLA subtyping ด้วย DNA typing kit ดังกล่าว อาจนำไปสู่การพบ alleles ใหม่ของ HLA antigen ได้ โดยทำการวิเคราะห์ด้วยวิธี sequence base typing ต่อไป

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